Amendments to the Claims

Claims 18, 30 and 58 were previously withdrawn.

Please amend claims 1, 20, 25, 44, 59 and 60 as indicated in the listing of claims.

Please cancel claims 6, 8-11, 26-27, 45, 53-54, 72-75 without prejudice or disclaimer.

Please add new claim 76-78.

Claims 5, 12-15, 38, 43, 62-71 were previously canceled.

The listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A set of primers, comprising at least 8 primers that selectively hybridize under highly stringent conditions to a nucleotide sequence flanking and within fifty nucleotides of each of polycystic kidney disease-associated protein-1 (PKD1) gene sequences set forth as

nucleotides 2043 to 4290 of SEQ ID NO:1,
nucleotides 17907 to 22489 of SEQ ID NO:1,
nucleotides 22218 to 26363 of SEQ ID NO:1,
nucleotides 26246 to 30615 of SEQ ID NO:1,.
nucleotides 30606 to 33957 of SEQ ID NO:1,
nucleotides 36819 to 37140 of SEQ ID NO:1
nucleotides 37329 to 41258 of SEQ ID NO:1, and
nucleotides 41508 to 47320 of SEQ ID NO:1,
or to a nucleotide sequence complementary to the PKD1 gene sequences,

wherein each primer of the set hybridizes to a nucleotide sequence flanking and within fifty nucleotides of one of the PKD1 gene sequences,

each of the primers comprising a 5' region and adjacent 3' region,

the 5' region comprising a nucleotide sequence that selectively hybridizes to a PKD1 gene sequence and, optionally, to a PKD1 gene homolog sequence, wherein the 5' region comprises at least ten contiguous nucleotides, and

the 3' region comprising a nucleotide sequence that selectively hybridizes to a PKD1 gene sequence, and not to a PKD1 gene homolog sequence, wherein the homolog sequence is a sequence having a high sequence identity to the PKD1 gene sequence,

provided the primer does not consist of a sequence as set forth in SEQ ID NO:11, SEQ ID NO:18, SEQ ID NO:52, or SEQ ID NO:60;

wherein the primers amplify at least a first and a second amplification product, and wherein two primers for the first amplification product are selected from the group consisting of SEQ ID NOs: 3, 4, 5 and 6, and two primers for the second amplification product are selected from the group consisting of SEQ ID NOs:19, 20, 21 and 22.

2. (Previously presented) The set of primers of claim 1,

wherein the 3' region comprises at least one 3' terminal nucleotide identical to a nucleotide that is 5' and adjacent to the nucleotide sequence of the PKD1 gene to which the 5' region of the primer can hybridize, and

wherein said 3' terminal nucleotide is different from a nucleotide that is 5' and adjacent to a nucleotide sequence of the PKD1 homolog to which the 5' region of the primer can hybridize.

3. (Previously presented) The set of primers of claim 2, wherein the 3' region comprises 2 to 4 3' terminal nucleotides.

4. (Previously presented) The set of primers of claim 2, comprising a 5' region of 14 to 18 nucleotides and a 3' region of 2 to 6 nucleotides.

5. (Canceled).

6. (Canceled).

7. (Previously presented) A set of primer pairs, each primer pair comprising a primer of claim 1, wherein the primer pairs selectively hybridize to SEQ ID NO:1 and can amplify a portion of SEQ ID NO:1 comprising about nucleotides 2043 to 4290; nucleotides 17907 to 22489; nucleotides 22218 to 26363; nucleotides 26246 to 30615; nucleotides 30606 to 33957; nucleotides 36819 to 37140; nucleotides 37329 to 41258; nucleotides 41508 to 47320; or a combination thereof.

8 to 11. (Canceled).

12 to 15. (Canceled).

16. (Previously presented) A solid matrix, comprising the set of primers of claim 1, wherein each of the primers is immobilized on the solid matrix.

17. (Original) The solid matrix of claim 16, which comprises a plurality of immobilized primers.

18. (Withdrawn) The solid matrix of claim 17, wherein the matrix comprises a plurality of primers, wherein said primers are degenerate with respect to one or more codons encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO:2.

19. (Original) The solid matrix of claim 16, wherein the solid matrix is a microchip.

20. (Currently amended) An isolated polynucleotide, comprising a contiguous sequence of at least ten nucleotides substantially identical to a nucleotide sequence of SEQ ID NO:1 or to a nucleotide sequence complementary thereto, wherein the ~~contiguous~~ nucleotide sequence ~~comprising with respect to~~ corresponds to nucleotide 3336 SEQ ID NO:1~~:~~ and wherein nucleotide 3336 is deleted

~~nucleotide 474, wherein nucleotide 474 is a T;~~

~~nucleotide 487, wherein nucleotide 487 is an A;~~

~~nucleotide 3110, wherein nucleotide 3110 is a C;~~

~~a position corresponding to nucleotide 3336, wherein nucleotide 3336 is deleted;~~

~~nucleotide 3707, wherein nucleotide 3707 is an A;~~

~~nucleotide 4168, wherein nucleotide 4168 is a T;~~

~~nucleotide 4885, wherein nucleotide 4885 is an A;~~

~~nucleotide 5168, wherein nucleotide 5168 is a T;~~

~~nucleotide 6058, wherein nucleotide 6058 is a T;~~

~~nucleotide 6078, wherein nucleotide 6078 is an A;~~

~~nucleotide 6089, wherein nucleotide 6089 is a T;~~

~~nucleotide 6195, wherein nucleotide 6195 is an A;~~

~~nucleotide 6326, wherein nucleotide 6326 is a T;~~

~~a position corresponding to nucleotides 7205 to 7211, wherein nucleotides 7205 to 7211 are deleted;~~

~~nucleotide 7376, wherein nucleotide 7376 is a C;~~

~~a nucleotide sequence corresponding to nucleotides 7535 to 7536, wherein a GCG nucleotide sequence is inserted between nucleotides 7535 and 7536;~~

~~nucleotide 7415, wherein nucleotide 7415 is a T;~~

~~nucleotide 7433, wherein nucleotide 7433 is a T;~~

~~nucleotide 7696, wherein nucleotide 7696 is a T;~~

~~nucleotide 7883, wherein nucleotide 7883 is a T;~~

~~nucleotide 8021, wherein nucleotide 8021 is an A;~~

~~a nucleotide sequence corresponding to nucleotide 8159 to 8160, wherein nucleotides 8159 to 8160 are deleted;~~

~~nucleotide 8298, wherein nucleotide 8298 is a G;~~

~~nucleotide 9164, wherein nucleotide 9164 is a G;~~

~~nucleotide 9213, wherein nucleotide 9213 is an A;~~

~~nucleotide 9326, wherein nucleotide 9326 is a T;~~

~~nucleotide 9367, wherein nucleotide 9367 is a T;~~

~~nucleotide 10064, wherein nucleotide 10064 is an A;~~

~~nucleotide 10143, wherein nucleotide 10143 is a G;~~

~~nucleotide 10234, wherein nucleotide 10234 is a C;~~

~~nucleotide 10255, wherein nucleotide 10255 is a T;~~

~~or a combination thereof~~.

21. (Original) A vector, comprising the polynucleotide of claim 20.

22. (Original) A host cell containing the vector of claim 20.

23. (Original) A solid matrix, comprising the polynucleotide of claim 20, wherein said polynucleotide is immobilized on the solid matrix.

24. (Original) The solid matrix of claim 23, wherein the polynucleotide comprises one of a plurality of polynucleotides, each of which is immobilized on the solid matrix.

25. (Currently amended) A method of detecting the presence or absence of a mutation in a PKD1 polynucleotide in a sample, the method comprising:

contacting nucleic acid molecules in a sample with a set of primer pairs, wherein the set of primer pairs is selected from the group consisting of SEQ ID NOs: 3, 4, 5, 6, 19, 20, 21 and 22, and wherein the ~~set consisting of~~ primer pairs ~~that~~ selectively hybridize to a PKD1 polynucleotide comprising SEQ ID NO: 1 and amplify a region of the PKD1 polynucleotide but not a PKD1 polynucleotide homolog ~~portion of SEQ ID NO: 1 comprising about nucleotides 2043 to 4290; nucleotides 17907 to 22489; nucleotides 22218 to 26363; nucleotides 26246 to 30615; nucleotides 30606 to 33957; nucleotides 36819 to 37140; nucleotides 37329 to 41258; nucleotides 41508 to 47320 under conditions suitable for amplification of a PKD1 polynucleotide by the primer pairs~~, thereby generating a PKD1-specific amplification product under said conditions; and

identifying the presence or absence of a mutation in the PKD1-specific amplification product, thereby detecting the presence or absence of a mutation in the PKD1 polynucleotide in the sample.

26 to 27. (Canceled).

28. (Original) The method of claim 25, wherein amplification is performed by a polymerase chain reaction.

29. (Original) The method of claim 25, wherein the PKD1 polynucleotide is a variant PKD1 polynucleotide.

30. (Withdrawn) The method of claim 29, wherein the variant PKD1 polynucleotide comprises a nucleotide sequence substantially identical to SEQ ID NO:1, wherein nucleotide 474 is a T; nucleotide 487 is an A; nucleotide 4884 is an A; nucleotide 6058 is a T; nucleotide 6195 is n A;

nucleotide 7376 is a C; nucleotide 7696 is a T; nucleotide 8021 is an A; nucleotide 9367 is a T; nucleotide 10143 is a G; nucleotide 10234 is a C; or nucleotide 10255 is a T.

31. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product comprises determining the nucleotide sequence of the amplification product.

32. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product comprises determining the melting temperature of the amplification product, and comparing the melting temperature to the melting temperature of a corresponding nucleotide sequence of SEQ ID NO:1.

33. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product is performed using denaturing high performance liquid chromatography.

34. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product is performed using matrix-assisted laser desorption time of flight mass spectrometry.

35. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product is performed using high throughput conformation-sensitive gel electrophoresis.

36. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product is performed by a method selected from single stranded conformation analysis, denaturing gradient gel electrophoresis, an RNAse protection assay,

allele-specific oligonucleotide detection, an allele-specific polymerase chain reaction, and an oligonucleotide ligation assay.

37. (Original) The method of claim 25, wherein identifying the presence or absence of a mutation in the amplification product is performed using a primer extension reaction assay,

wherein the primer extension reaction is performed using a detectably labeled primer and a mixture of deoxynucleotides and dideoxynucleotides, and

wherein the primer and mixture are selected so as to enable differential extension of the primer in the presence of a wild type PKD1 polynucleotide as compared to a mutant PKD1 polynucleotide.

38. (Canceled).

39. (Original) The method of claim 25, wherein the method is performed in a high throughput format using a plurality of samples.

40. (Original) The method of claim 39, wherein plurality of samples are in an array.

41. (Original) The method of claim 40, wherein the array comprises a microtiter plate.

42. (Original) The method of claim 40, wherein the array is on a microchip.

43. (Canceled).

44. (Currently amended) A method of identifying a subject at risk for a PKD1-associated disorder, the method comprising:

contacting nucleic acid molecules in a sample from a subject with ~~the~~ a set of primer pairs, wherein the sample is contacted with a first set of primer pairs selected from the group consisting of SEQ ID NOs: 3, 4, 5 and 6, and the sample is subsequently contacted with a second set of primer pairs selected from the group consisting of SEQ ID NOs: 19, 20, 21 and 22, and wherein the ~~set consisting of~~ primer pairs ~~that~~ selectively hybridize to a PKD1 polynucleotide comprising SEQ ID NO: 1 and amplify a ~~portion~~ region of SEQ ID NO: 1 ~~comprising about nucleotides 2043 to 4290; nucleotides 17907 to 22489; nucleotides 22218 to 26363; nucleotides 26246 to 30615; nucleotides 30606 to 33957; nucleotides 36819 to 37140; nucleotides 37329 to 41258; nucleotides 41508 to 47320~~ under conditions suitable for amplification of ~~a~~ the PKD1 polynucleotide but not a PKD1 polynucleotide homolog by the primer pair, thereby generating ~~an~~ a first and second amplification product; and

detecting the presence or absence of a mutation indicative of a PKD1-associated disorder in the second amplification product,

wherein the absence of the mutation identifies the subject a not at risk for a PKD1-associated disorder, and

wherein the presence of the mutation identifies the subject as at risk for a PKD1-associated disorder.

45. (Canceled).

46. (Original) The method of claim 44, wherein the PKD1-associated disorder is autosomal dominant polycystic kidney disease.

47. (Original) The method of claim 44, wherein the PKD1-associated disorder is acquired cystic disease.

48. (Original) The method of claim 44, wherein the method is performed in a high throughput format.

49. (Original) The method of claim 44, wherein detecting the presence or absence of a mutation indicative of a PKD1-associated disorder in the amplification product comprises accumulating data representative of the presence or absence of the mutation.

50. (Original) The method of claim 49, wherein the data is formatted into a report indicating whether a subject is at risk of a PKD1-associate disorder.

51. (Original) The method of claim 50, further comprising transmitting the report to a user.

52. (Original) The method of claim 51, wherein transmitting the report comprises sending the report over the internet, by facsimile or by mail.

53 to 54. (Canceled).

55. (Original) The method of claim 53, detecting the presence or absence of the mutation comprises determining the nucleotide sequence of the amplification product, and comparing the nucleotide sequence to a corresponding nucleotide sequence of SEQ ID NO:1.

56. (Original) The method of claim 53, wherein detecting the presence or absence of the mutation comprises determining the melting temperature of the amplification product, and comparing the melting temperature to the melting temperature of a corresponding nucleotide sequence of SEQ ID NO:1.

57. (Original) The method of claim 53, wherein detecting the presence or absence of the mutation is performed using denaturing high performance liquid chromatography.

58. (Withdrawn) The method of claim 44, wherein the mutation indicative of a of PKD1 associated disorder comprises a nucleotide sequence substantially identical to SEQ ID NO:1, wherein nucleotide 3110 is a C; nucleotide 8298 is a G; nucleotide 9164 is a G; nucleotide 9213 is an A; nucleotide 9326 is a T; or nucleotide 10064 is an A.

59. (Currently amended) The method of claim 44, wherein the mutation indicative of a of PKD1 associated disorder comprises a nucleotide sequence substantially identical to SEQ ID NO:1, wherein nucleotide 3336 is deleted~~; nucleotide 3707 is an A; nucleotide 5168 is a T; nucleotide 6078 is an A; nucleotide 6089 is a T; nucleotide 6326 is a T; nucleotides 7205 to 7211 are deleted; nucleotide 7415 is a T; nucleotide 7433 is a T; nucleotide 7883 is a T; or nucleotides 8159 to 8160 are deleted; or wherein a GCG nucleotide sequence is inserted between nucleotides 7535 and 7536~~.

60. (Currently amended) A method of diagnosing a PKD1-associated disorder in a subject, the method comprising:

amplifying a portion of a PKD1 ~~polynucleotide~~ gene but not a PKD1 gene homolog in a nucleic acid sample from a subject with ~~the~~ a first set of primer pairs, wherein the first set of primer pairs is selected from the group consisting of SEQ ID NOs: 3, 4, 5 and 6 and wherein the ~~set consisting of~~ primer pairs ~~that~~ selectively hybridize to SEQ ID NO: 1 and amplify a ~~portion~~ region of SEQ ID NO: 1 ~~comprising about nucleotides 2043 to 4290; nucleotides 17907 to 22489; nucleotides 22218 to 26363; nucleotides 26246 to 30615; nucleotides 30606 to 33957; nucleotides 36819 to 37140; nucleotides 37329 to 41258; nucleotides 41508 to 47320~~ to obtain a first amplification product;

amplifying the first amplification product with at least a second set of primer pairs to obtain a nested amplification product, wherein the second set of primers pairs is selected from the group consisting of SEQ ID NO:19, 20, 21 and 22, and wherein the second set of primer pairs is suitable for performing nested amplification of the first amplification product; and

determining whether the nested amplification product has a mutation associated with a PKD1-associated disorder,

wherein the presence of a mutation associated with a PKD1-associated disorder is indicative of a PKD1-associated disorder, thereby diagnosing a PKD1-associated disorder in the subject.

61. (Original) The method of claim 60, wherein the method is performed in a high throughput format using a plurality of nucleic acid samples.

62-71. (Canceled).

72. to 75. (Canceled).

76. (New) The method of claim 25, wherein prior to identifying the presence or absence of a mutation in the PKD1-specific amplification product, the amplification product is serially diluted to remove genomic contamination.

77. (New) The method of claim 44, wherein prior to detecting the presence or absence of a mutation in the PKD1-specific amplification product, the amplification product is serially diluted to remove genomic contamination.

78. (New) The method of claim 60, wherein prior to obtaining the nested amplification product, the first amplification product is serially diluted to remove genomic contamination.